General

Guideline Title

Stem cell transplantation in myelodysplastic syndromes and acute myeloid leukemia.

Bibliographic Source(s)

Kouroukis CT, Rumble RB, Walker I, Bredeson C, Schuh A. Stem cell transplantation in myelodysplastic syndromes and acute myeloid leukemia. Toronto (ON): Cancer Care Ontario (CCO); 2012 Mar 29. Various p. (Recommendation report; no. SCT-3). [35 references]

Guideline Status

This is the current release of the guideline.

The RECOMMENDATION REPORT, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

Recommendations

Major Recommendations

Myelodysplastic Syndrome (MDS)

- Allogeneic transplantation is an option for patients with MDS. This is the only potentially curative therapy for MDS.
- Autologous stem cell transplantation (ASCT) is not recommended for patients with MDS.

Acute Myeloid Leukemia (AML)

First Complete Remission

- Allogeneic transplantation is a treatment option for selected patients with AML in first complete remission (CR1) with high-risk features including intermediate or high-risk cytogenetic or molecular phenotypes, high-risk clinical features at presentation, and secondary or treatment-related AML.
- ASCT is not recommended for patients with AML in first complete remission.

Beyond First Complete Remission

- Allogeneic transplantation is the recommended option for eligible patients with AML who achieve a second or subsequent remission.

- There is insufficient evidence to support the use of ASCT for patients with AML in the second or subsequent remission.
- Autologous transplantation is recommended for acute promyelocytic leukemia (APL) in a molecularly-negative second remission.
- Select patients with AML not in remission may derive benefit from allogeneic transplant.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Myelodysplastic syndrome (MDS)
- Acute myeloid leukemia (AML)

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Hematology

Oncology

Intended Users

Physicians

Guideline Objective(s)

- To evaluate the role of stem cell transplantation (SCT) in the treatment of myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML)
- To review the most current evidence comparing treatment modalities that include an SCT component
- To make a series of clinical recommendations to inform clinicians, patients, and other stakeholders of the treatment options available

Target Population

All adult patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) being considered for treatment that includes either blood or bone marrow transplantation

Interventions and Practices Considered

1. Allogeneic transplantation
2. Autologous stem cell transplantation (ASCT)

Major Outcomes Considered

- Survival (three-year overall, median, overall, three-year disease-free, leukemia-free, relapse-free)
- Three-year treatment-related mortality
- Acute graft-versus-host disease

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Strategy

Myelodysplastic Syndrome (MDS)

The MEDLINE (OVID) database (1996 through October [week two] 2010) was systematically searched for evidence on October 21, 2010 using the strategy that appears in Appendix A of the original guideline document. A total of 89 hits were obtained, and after excluding irrelevant papers according to a title and abstract review, 21 were ordered for full-text review. Of these 21, only four met the inclusion criteria and were retained.

Acute Myeloid Leukemia (AML)

The MEDLINE (OVID) database (1996 through October [week one] 2010) was systematically searched for evidence on October 21, 2010 using the strategy that appears in Appendix B of the original guideline document. A total of 211 hits were obtained, and after excluding irrelevant papers according to a title and abstract review, 64 were ordered for full-text review. Of these 64, only 17 met the inclusion criteria and were retained.

Study Selection Criteria

Articles were selected if they were the following:

1. Systematic reviews (SRs) with or without meta-analysis or clinical practice guidelines if evidence was obtained with a systematic review.
2. Fully published randomized controlled trials (RCTs) on patients with MDS or AML who received stem cell transplantation (SCT) that reported on survival outcomes and/or quality of life (QoL).
3. Fully published non-randomized studies on patients with MDS or AML who received SCT that had an appropriate comparison group that reported on survival outcomes or QoL.
4. Reports published in English only.

Number of Source Documents

- Myelodysplastic syndrome: A systematic review (SR), a National Comprehensive Cancer Network (NCCN) clinical practice guideline (CPG), and two retrospective cohort studies were obtained.
- Acute myeloid leukemia: Seventeen papers were obtained, comprising three SRs, three CPGs, three meta-analyses, one prospective cohort study, and seven retrospective cohort studies.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Synthesizing the Evidence

While no pooling was planned, it would be considered if data allow.

Assessment of Study Quality

The quality of the included evidence was assessed as follows. For systematic reviews that would be used as the sole evidence base for the recommendations, or where solely a systematic review (SR) supported any specific recommendation, the Assessment of Multiple Systematic Reviews (AMSTAR) tool would be used to assess quality. For clinical practice guidelines (CPGs), the Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument would be used, but only if an adaptation of the recommendations was being considered.

Where recommendations from CPGs were not adapted, the evidence base in those CPGs would be informally assessed for completeness, and any relevant evidence within would be considered as a basis for recommendations in this report. Any meta-analysis would be assessed for quality using criteria similar to that used for randomized controlled trials (RCTs), where appropriate. RCTs would be assessed for quality by examining the following seven criteria: the method of randomization, reporting of blinding, the power and sample size calculation, length of follow-up, reporting on details of the statistical analysis, reporting on withdrawals to treatment and other losses to follow-up, and reporting on the sources of funding for the research. Comparative, but non-randomized, evidence would be assessed according to the full reporting of the patient selection criteria, the interventions each patient received, and all relevant outcomes.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

Evidence in this report included prospective cohort studies, retrospective cohort studies, systematic reviews with or without meta-analysis, and clinical practice guidelines.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- One systematic review comprising a total of 22 studies demonstrated a long-term curative outcome for related, unrelated, either or unspecified allogeneic stem cell transplantation (alloSCT).
- One systematic review, comprising 24 clinical studies involving 6,007 patients with acute myeloid leukemia (AML) in first complete remission (CR1) comparing alloSCT, autologous SCT (ASCT), chemotherapy (CT), or any combination of the three, found a significant relapse-free survival (RFS) and overall survival (OS) benefit associated with alloSCT. That review performed subgroup analyses for both recurrence or RFS and OS according to patient risk (good, intermediate, or poor risk). Significant benefits in favour of alloSCT for both intermediate and poor risk patients ($p<0.01$) were detected, but no difference was detected with good risk patients. The OS subgroup analysis also detected significant benefits in favour of alloSCT for intermediate and poor risk patients ($p<0.01$) but not for good risk patients.
- One meta-analysis, that pooled data from two trials (AML 96 and AML 02) that compared alloSCT with ASCT with CT, including a total of 708 patients, detected significant differences in favour of alloSCT for both OS and leukemia-free survival (LFS) at two years. In a multivariate analysis, factors associated with better OS and longer LFS were being younger ($p=0.008$) and receiving an allogeneic transplant.
- One prospective cohort study found significant benefits in favour of alloSCT compared with ASCT in the relative risk for eight-year disease-free survival (DFS).

Potential Harms

Stem cell transplantation (SCT) is associated with graft versus host disease (GVHD) and treatment-related mortality.

Qualifying Statements

Qualifying Statements

- The patient selection process and the ultimate decision to perform a stem cell transplantation (SCT) should take into account not only disease-related characteristics, but also co-morbidities and patient preferences. Patients with myelodysplastic syndrome and acute myeloid leukemia should be referred to a transplant centre for transplant assessment.
- Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Kouroukis CT, Rumble RB, Walker I, Bredeson C, Schuh A. Stem cell transplantation in myelodysplastic syndromes and acute myeloid leukemia. Toronto (ON): Cancer Care Ontario (CCO); 2012 Mar 29. Various p. (Recommendation report; no. SCT-3). [35 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Mar 29

Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

Guideline Developer Comment

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

Source(s) of Funding

The Program in Evidence-based Care (PEBC) is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Guideline Committee

Hematology Disease Site Group

Composition of Group That Authored the Guideline

For a current list of past and present members, please see the Cancer Care Ontario Web site .

Financial Disclosures/Conflicts of Interest

The authors of this recommendation report disclosed potential conflicts of interest relating to the topic of this special advice report. Three of the authors reported no conflicts (TK, RBR, CB). One author reported being a principal investigator (PI) on a related trial (IW), and another reported attending an out-of-country request hearing as a patient advocate (AS).

Guideline Status

This is the current release of the guideline.

The RECOMMENDATION REPORT, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site .

Availability of Companion Documents

The following are available:

- Stem cell transplantation in myelodysplastic syndromes and acute myeloid leukemia. Summary. Toronto (ON): Cancer Care Ontario; 2012 Mar 29. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario (CCO) Web site .
- Program in evidence-based care handbook. Toronto (ON): Cancer Care Ontario (CCO); 2012. 14 p. Electronic copies: Available in PDF from the CCO Web site .

Patient Resources

None available

NGC Status

This summary was completed by ECRI Institute on September 6, 2013.

Copyright Statement

Disclaimer

NGC Disclaimer